

# Hypophysectomy for Palliation of Breast Cancer

## With Especial Reference to Surgical Technique

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SUCCESSFUL total hypophysectomy was probably first performed in 1951 by Olivecrona<sup>2</sup> in Sweden, who operated on a 30-year-old man with diabetes mellitus. Later, Luft and Olivecrona reported on a series of hypophysectomies, including nine which were done on patients with cancer of the breast, some of whom showed definite improvement.<sup>3</sup> Soon after the publication of Olivecrona's first series, Ray and Pearson in New York began an objective study of the effects of hypophysectomy on neoplastic disease and the endocrine system. In a series of 74 women with advanced cancer of the breast, 67 survived and 36 of them (53.7 per cent) had remission.<sup>6</sup> For those with remission the average survival of 9.3 months compared with 4.4 months for those who had no remission.\*

It has been known for some time that endocrine treatment of metastatic cancer of the breast induces remissions in about half the cases. Just why tumors in premenopausal women respond to testosterone and those in postmenopausal respond to estrogens has never been adequately explained. Luft's interpretation was that the phenomenon involved the inhibitory action of the estrogens on the hypophysis.<sup>4</sup> Pearson and co-workers reported stimulation of cancer growth by beef pituitary somatotropin in a patient who had had a regression of tumor growth for three months after hypophysectomy.<sup>5</sup> Therefore, as Luft has stated, "The purpose of hypophysectomy is two-fold: First, to achieve a complete sex hormone control by elimination of the gonadotropic and adrenocorticotrophic hormones, and, secondly, to eliminate other pituitary hormones which are, or can be, associated with the growth of cancer of the breast and prostate."<sup>4</sup>

### Material

Selection of the 19 patients in whom the authors carried out hypophysectomy was based on the expe-

• In a series of 19 patients who had hypophysectomy for palliation of cancer of the breast, all had striking relief of pain. Objective evidence of remission of disease was observed in ten patients.

The survival time after operation averaged 19.8 months for patients who had remission and 2.1 months for patients who did not.

Results were better in patients who had had cancer for a long time before operation than in those who had had the disease a relatively short time. Also it was noted that results were better in patients who had had preoperative response to endocrine therapy than in those who had not. Hence these factors may be considered in selection of patients for hypophysectomy.

riences of Ray and Pearson who looked upon patients with intracerebral or extensive liver metastasis or pronounced cachexia as too poor risks and as having too limited a life expectancy to warrant operation.

### Surgical Technique

Refinements in technique that have been evolved over the past three years have immensely facilitated complete removal of the pituitary gland, especially in patients with brain edema or prefixed chiasms. The position advocated by Shelden and co-workers (cited by Freshwater and associates<sup>1</sup>) is recommended: A prone position with blanket rolls on either side of the thorax, the neck sharply extended and the cheeks resting on bilateral cup head rests with the body well strapped down by multiple adhesive strips and the feet resting on a fixed footrest so that the table may then be inclined to a 45 degree angle, putting the patient's face and forehead in a vertical plane directly facing that of the operator. This position results in an almost complete emptying of venous spaces around the sella. It also permits a better view of the sella and pituitary stalk. With the patient under intratracheal trile-ne-nitrous oxide anesthesia, a transverse incision is made at the hairline of the scalp to obtain subperiosteal exposure of the frontal bone. With a 1½-inch trephine placed so that one edge is slightly over the midline, in order to approach the sella as close to the falx as possible, a bone button is removed.

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\*Ray has now carried out hypophysectomy in more than 200 patients, accumulating a great knowledge of the effects of this operation on breast cancer growth and on other endocrine dysfunctions; and he continues of the opinion that hypophysectomy is the treatment of choice in the majority of cases of metastatic breast carcinoma. He believes this treatment may well replace other forms of endocrine operation and medication.<sup>7</sup>

(The author formerly used bilateral supraorbital 1½-inch trephine exposures on either side of the frontal sinus, permitting visualization of both walls of the sella turcica, but direct traversal of the frontal sinus, as recommended by Ray, is simpler and quite satisfactory.)

An effort is made to keep intact the mucous membrane by packing the area below the bone button with strips of Gelfoam. There appears to be little danger of permanent rhinorrhea or infection with this approach; it has been used by one of the authors (WBS) many times in fractional undercutting lobotomy procedures. The sella is approached directly alongside the falx, the procedure usually involving sectioning one olfactory nerve after incising the tip of the dura in an inverted T incision, retracting the frontal lobe upward and inserting a thin metal "tunnel" retractor as advocated by Shelden and Pudenz. The tunnel retractor consists of a thin sheet of lead or aluminum cut in the shape of a trapezoid and bent to form three sides of a tunnel which is then slid in along the roof of the orbit holding the frontal lobe away from the floor. It permits adequate visualization of the optic chiasm. A parallel beam headlight is advocated for viewing the depths of the exposure.

With the area exposed, the pituitary stalk is identified and cut close to the diaphragm sella in order to lessen the degree of postoperative diabetes insipidus. The diaphragm sellae is then torn (rather than incised in a cruciate fashion by use of a nerve hood and "cutting" current) to expose the pituitary gland. Should there be a prefixed chiasm, as there is in about one-third of the cases, the space between the chiasm and tuberculum sellae is too narrow to permit good visualization of the pituitary gland. To meet the situation, after reflecting the dura by means of a T incision, the bone of the posterior tuberculum sellae and the anterior wall of the sella turcica are removed with a dental chisel, unroofing the sphenoid sinus and its septum. The mucous membrane is pushed downward with Gelfoam packing and muscle stamps; the optic nerves are elevated by inserting cotton pads under them; the diaphragm sellae is torn open and the circular sinus and anterior dural wall of the sella are coagulated and incised, thereby both unroofing and unwalling the sella turcica anteriorly and exposing the pituitary gland transsphenoidally and anteriorly.

When the pituitary has been thus exposed from above and, if necessary, anteriorly, it is freed in its cavity by use of blunt angled pituitary dissectors developed by Olivecrona, and an effort is made to remove it whole by packing cotton pads around and underneath it, causing it to extrude en masse. Frequently, however, this is impossible and it is

TABLE 1.—Operative Morbidity in 19 Cases After Hypophysectomy

	Number	Per Cent
Diabetes insipidus .....	19	100
Rhinorrhea .....	7	36.8
Optic nerve injury.....	2	10.5
Convulsions (first postoperative day).....	1	5.3

necessary to use the sharp angled pituitary ring curets, developed by Ray, for piecemeal removal. The lateral, posterior and anterior dural walls of the sella are thoroughly scraped and in some cases even removed. Bleeding from the cavernous sinus is easily stanching by Gelfoam. With such thorough removal of all contents under direct vision, we have not used Zenker's solution to kill remaining gland cells, although other surgeons commonly inject it into cotton pads within the sella, using suction at the same time to prevent contact with the optic nerves.

This detailed account of technique is given because total removal of every fragment of pituitary gland, although most difficult, is most necessary for therapeutic benefit. Even with meticulous technique, nests of pituitary cells may sometimes be observed microscopically in the dural lining of patients who die. In the process of closing the wound, Gelfoam is placed in the sella, muscle stamps are left in any opening made in the sphenoid sinus, the "tunnel" retractor is removed so that the frontal lobe can again make contact with the floor of the anterior fossa, the dura is closed loosely, the bone button is replaced without wiring and covered with a layer of thinnest tantalum mesh for cosmetic reasons, the frontal flap is closed and a new type of Ace sponge rubber 3-inch bandage is wrapped snugly overlying the supraorbital flap in order to prevent eyelid edema. Rhinorrhea for two or three days is not uncommon, but in no case in the author's series did it continue for longer than five days.

The preoperative and postoperative management has been thoroughly discussed by other observers.<sup>3,4,5,6</sup> In this series the therapy outlined by Ray and Pearson<sup>6</sup> was followed.

There was one death in the series attributable to operation. This was in a difficult case in which the hypothalamus was traumatized. The patient was in coma postoperatively and died in coma on the 23rd postoperative day. Data on operative morbidity is shown in Table 1.

#### Results and Comment

Three patients had unsuspected metastatic cancer in the pituitary gland. In each of these patients, removal of the gland caused exorbitant bleeding.

All the patients had striking subjective relief of pain postoperatively, appreciably lessening their need for narcotics. Of the 19 patients, ten showed

some objective evidence of remission of disease. Five of the 19 patients were still living, from one to six months after operation, two of them asymptomatic, two improving and one regressing. Twelve patients had had endocrine therapy or oophorectomy before hypophysectomy, five without relief. The seven who were helped by those means were also helped both objectively and subjectively by hypophysectomy (Table 2). Of the five not benefited by endocrine therapy or oophorectomy, one had relief of pain without objective changes after hypophysectomy and one had objective improvement as well. This tends to suggest that a trial of hormones might be of value in selecting patients for hypophysectomy.

Luft and Olivecrona said that they observed no favorable response in women over 60 years of age. Ray and Pearson reported benefit in several women above that age.<sup>6</sup> Of two women over 60 years of age in the present series, one had a fair result and the other showed no improvement.

The length of time the disease existed before hypophysectomy seemed to be related to the survival time (Table 3) after operation. Patients in whom remission occurred had had cancer for an average of 4.9 years before hypophysectomy, and those without remission had had the disease an average of 2.7 years. As did other investigators, we attempted, without success, to find some correlation between the results of hypophysectomy and other factors such as age of the patient, tumor cell type, response to x-ray therapy and extent of disease.

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**TABLE 2.—Data on Relation of Results of Hypophysectomy to Preoperative Endocrine Therapy and Oophorectomy**

Treatment	Total	Improved by Therapy	Posthypophysectomy Remission
Endocrine alone .....	9	4	4
Endocrine and oophorectomy .....	3	3	3
Total .....	12	7	7

**TABLE 3.—Survival After Hypophysectomy**

	Number	Average Survival	Still Living
With remission .....	10	19.8 months	4
Without remission.....	9	2.1 months	1

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